REMARKS

With entry of this amendment, claims 1-30 and 35-61 are pending in the application. By this Amendment claims 31-34 have been canceled without prejudice, and claims 1, 3, 5, 6, 15, 16, 17, 22, 24, 29, 30, 36, and 3961 have been amended for clarity. Additional subject matter in the application is maintained through continued prosecution of the parent application (by contemporaneously filed RCE) or in contemporaneously-filed Continuation Applications (Attorney Docket Numbers NPCI-0292, and NPCI-0293). By these combined submissions, no subject matter is relinquished in the present application and no accession is made concerning issues of patentability previously advanced by the Office. No new matter has been added to the application.

The instant submission and co-filed RCE and Continuation Applications are presented pursuant to an Examiner Interview held between representatives of the Office, Examiner Jennifer Kim and Primary Examiner Theodore Criares, and Applicants' representatives, Jeffrey King and Dr. Steven Quay, on December 3, 2001. Applicants are grateful to Examiner Kim and Primary Examiner Criares for their courtesy and patience during this lengthy and detailed Interview.

The Interview covered in depth several main aspects of the invention disclosed in the present application. Briefly, these aspects that were discussed in the Interview included:

(I) Intranasal compositions and dosage forms of dopamine receptor agonists that are effective for treatment of sexual dysfunction in mammals without unacceptable adverse side effects;

(II) Intranasal compositions and dosage forms of dopamine receptor agonists as provided in aspect (I), above, further characterized by having a novel pH in the range of about 3.0 to about 3.5--yielding unexpected stabilization of the subject compositions and dosage forms;

(III) Intranasal compositions and dosage forms of dopamine receptor agonists as provided in aspect (I), above, further characterized as comprising "a plurality of reducing

agents"--yielding independent, unexpected stabilization of the subject compositions and dosage forms; and

(IV) Intranasal compositions and dosage forms of dopamine receptor agonists as provided in aspect (I), above, further characterized as having an effective dosage amount of below about 2.0 mg, or below about 1.0 mg--yielding unexpected efficacy without unacceptable adverse side effects.

For clarity and efficiency of further prosecution, it was agreed during the Interview that each of the foregoing aspects of Applicants' technology would be presented for separate further examination, as has been achieved by this submission and co-filing of the above-noted RCE and Continuation Applications.

The instant submission presents for further examination the subject matter identified as aspect (I), above, relating to aqueous intranasal compositions and dosage forms of dopamine receptor agonists—yielding unexpected results relating to efficacy for treatment of sexual dysfunction in mammals without unacceptable adverse side effects. The remaining subject matter identified as aspects (I), (II), and (IV) above is substantially maintained in the contemporaneously filed RCE and Continuation Applications, and thus is not effectively canceled or withdrawn from consideration through the instant course of prosecution.

With respect to the claims pending in the instant application, Applicants presented detailed evidence and remarks during the Interview that are believed to establish unexpected results for the claimed invention over the art of record—particularly in terms of unexpected efficacy of an aqueous dopamine agonist formulation without adverse side effects. On this basis, and in further reference to therecord of submissions in the parent application, including the Declaration of Jorge de Meireles filed on April 4, 2001, Applicants respectfully submit that the instantly claimed subject matter is patentable under 35 U.S.C. § 103(a) over the art of record, including the cited El-Rashidy et al. (U.S. Patent No. 5770606), Merkus (U.S. Patent No. 5756483), and Illum (WO 99/27905) references.

Applicants note that all of the subject matter embodied in the present claims has been previously considered in detail and through the prior course of prosecution in the parent application with respect to novelty and compliance with 35 U.S.C. § 112, First and

Second paragraphs. Thus, the only issue believed to be remaining in this application is patentability under 35 U.S.C. § 103. Applicants respectfully submit that this issue was advanced during the course of the above-noted Interview and prosecution in the parent application, although Applicants reserve the right to present further evidence and remarks in this context.

CONCLUSION

Applicants believe that all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-332-1380.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

Date: 1/31/02

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Version With Markings To Show Changes Made

IN THE SPECIFICATION:

At page 1, between the Title and "Background of the Invention" heading, please insert the following new section:

--Cross References to Related Applications

This application is a Continuation of U.S. Application Serial No. 09/334,304, filed June 16, 1999, which claims the benefit of U.S. Provisional Application No. 60/096,545, filed August 14, 1998.—

IN THE CLAIMS:

Claims 31-34 have been canceled, without prejudice.

Claims 1, 3, 5, 6, 15, 16, 18, 22, 24, 29, 30, 36, 39, and 40-61have been amended as follows:

1. (Amended) A method of ameliorating [male erectile] sexual dysfunction in a mammal comprising nasally administering a therapeutically effective amount of a dopamine receptor agonist in an aqueous formulation for intranasal delivery to said mammal before, during or after sexual activity which is [sufficient to induce an erection] intranasally effective to alleviate said sexual dysfunction without causing substantial intolerable adverse side effects to said mammal.

2. The method of Claim 1, wherein said dopamine receptor agonist is selected from the group consisting of apomorphine, chemically modified equivalents and pharmaceutical salts thereof.

3. (Amended) A pharmaceutical composition for treating [male erectile] sexual dysfunction in a mammal comprising a therapeutically effective amount of a dopamine receptor agonist in [combination with a nasal delivery system] in an aqueous formulation for intranasal delivery, wherein said pharmaceutical composition [does not cause] is intranasally effective to alleviate said sexual dysfunction without causing substantial intolerable adverse side effects in said mammal.

4. The pharmaceutical composition of Claim 3, wherein said dopamine receptor agonist is apomorphine.

5. (Amended) The pharmaceutical composition of Claim 4, wherein said apomorphine is dispersed in an aqueous [or non-aqueous] spray formulation.

6. (Amended) The pharmaceutical composition of Claim 4, wherein said [nasal delivery system] aqueous formulation for intranasal delivery comprises a buffer to maintain the pH of said dopamine receptor agonist, a pharmaceutically acceptable thickening agent and a humectant.

7. The pharmaceutical composition of Claim 6, further comprising one or more pharmaceutical excipients.

8. The pharmaceutical composition of Claim 7, further comprising a pharmaceutically acceptable preservative.

9. The pharmaceutical composition of Claim 6, wherein said buffer is selected from the group consisting of acetate, citrate, prolamine, carbonate and phosphate buffers.

10. The pharmaceutical composition of Claim 6, wherein said thickening agent is selected from the group consisting of methyl cellulose, xanthan gum, carboxymethyl cellulose, hydroxypropyl cellulose, carbomer, polyvinyl alcohol, alginates, acacia, chitosans and combinations thereof.

11. The pharmaceutical composition of Claim 6, wherein said humectant is selected from the group consisting of sorbitol, glycerol, mineral oil, vegetable oil and combinations thereof.

12. A method of treating erectile dysfunction in a male mammal comprising nasally administering the composition according to Claim 3.

13. The pharmaceutical composition of Claim 3, wherein said dopamine receptor agonist is selected from the group consisting of apomorphine, chemically modified equivalents and pharmaceutical salts thereof.

14. The pharmaceutical composition of Claim 13, wherein said chemically modified equivalents comprise a pro-drug.

15. (Amended) A [nasally administered] pharmaceutical composition for treating male or female sexual dysfunction in a mammalian subject comprising a therapeutically effective amount of a dopamine receptor agonist dispersed in an aqueous formulation for intranasal delivery comprising a buffer to maintain [its pH] a pH of the formulation, a pharmaceutically acceptable thickening agent and a humectant, wherein said [nasally administered] pharmaceutical composition is intranasally effective to alleviate said sexual dysfunction and does not cause substantial intolerable adverse side effects when administered to said mammal.

16. (Amended) The [nasally administered] pharmaceutical composition of Claim 15, wherein said dopamine receptor agonist is selected from the group including apomorphine, chemically modified equivalents and pharmaceutical salts thereof.

17. (Amended) The [nasally administered] pharmaceutical composition of Claim 16, wherein said chemically modified equivalents comprise a pro-drug.

18. A method of treating impotence and male erectile dysfunction in a human in need of such treatment comprising administering to a nasal membrane of said human an effective amount of a composition according to Claim 15.

19. A method of treating male erectile without causing substantial intolerable adverse side effects in a mammal comprising administering into a nasal cavity of said mammal a therapeutically effective dosage of a dopamine receptor agonist in combination with a nasal delivery system comprising a pharmaceutically acceptable buffer, a thickening agent and a humectant.

20. The method of Claim 19, wherein said dopamine receptor agonist is selected from the group consisting of apomorphine, chemically modified equivalents and pharmaceutical salts thereof.

21. The method of Claim 20, wherein said chemically modified equivalents comprise a pro-drug.

22. (Amended) A method of administering a therapeutically effective amount of a dopamine receptor agonist to a mammal through a nasal membrane thereof for treatment of male or female sexual dysfunction in said mammal comprising delivering to said nasal membrane a therapeutically effective amount of said dopamine receptor agonist which does not cause substantial intolerable adverse side effects in said mammal, wherein said dopamine receptor agonist is dispersed in [a nasal delivery system] an aqueous formulation for intranasal delivery comprising a pharmaceutically acceptable a buffer, a thickening agent and a humectant.

23. The method of Claim 22, wherein said dopamine receptor agonist is effective for the treatment of male erectile dysfunction in a mammal.

24. (Amended) An intranasal dosage unit for treating impotency or erectile dysfunction in a mammal comprising an effective amount of a dopamine receptor agonist in [combination with an intranasal carrier] an aqueous formulation for intranasal delivery comprising a buffer, wherein said dosage unit does not cause substantial intolerable adverse side effects in said mammal and an erection is produced in said mammal within about 60 minutes of administering said dosage unit to a nasal mucosa of said mammal.

25. The intranasal dosage unit of Claim 24, wherein said erection is produced within about 45 minutes.

26. The intranasal dosage unit of Claim 24, wherein said erection is produced within about 30 minutes.

27. The intranasal dosage unit of Claim 24, wherein said erection is produced within about 15 minutes.

28. The intranasal dosage unit of Claim 24, wherein said erection is produced in less than about 15 minutes.

29. (Amended) The intranasal dosage unit of Claim 24, wherein said [intranasal carrier is an] aqueous [solution] formulation is administered to said mammal as an aqueous spray.

30. (Amended) The intranasal dosage unit of Claim 29, wherein said aqueous [solution] formulation is selected from the group consisting of aqueous gels, aqueous suspensions, aqueous liposomal dispersions, aqueous emulsions, aqueous microemulsions and combinations thereof.

35. The intranasal dosage unit of Claim 24, further comprising an excipient having bio-adhesive properties.

36. (Amended) The intranasal dosage unit of Claim 24, wherein said buffer is selected to have a pH of from about 3 to about [10]3.5.

37. The intranasal dosage unit of Claim 24, further comprising a humectant.

38. The intranasal dosage unit of Claim 37, wherein said humectant is selected from the group consisting of soothing agents, membrane conditioners, sweeteners and combinations thereof.

39. (Amended) A [nasally administered] pharmaceutical composition [for treating male erectile dysfunction in a mammal comprising a therapeutically effective amount of a] according to claim 3, wherein said dopamine receptor agonist [which] has been dispersed [in a system] with a solubilizing agent to improve its solubility.

40. (Amended) The [nasally administered] pharmaceutical composition of Claim 39, wherein said dopamine receptor agonist is selected from the group consisting of apomorphine, chemically modified equivalents and pharmaceutical salts thereof.

41. (Amended) The [nasally administered] pharmaceutical composition of Claim 39, wherein said system comprises glycerin.

42. (Amended) The [nasally administered] pharmaceutical composition of Claim 39, wherein said [system] solubilizing agent comprises a glycol derivative.

43. (Amended) The [nasally administered] pharmaceutical composition of Claim 42, wherein said glycol derivative is propylene glycol.

44. (Amended) The [nasally administered] pharmaceutical composition of Claim 42, wherein said glycol derivative is polyethylene glycol.

45. (Amended) The [nasally administered] pharmaceutical composition of Claim 39, wherein said [system] solubilizing agent comprises a sugar alcohol.

46. (Amended) The [nasally administered] pharmaceutical composition of Claim 39, wherein said [system] solubilizing agent comprises propylene glycol and glycerin.

47. (Amended) The [nasally administered] pharmaceutical composition of Claim 39, wherein said [system] solubilizing agent comprises ascorbic acid and water.

48. (Amended) The [nasally administered] pharmaceutical composition of Claim 39, wherein said [system] solubilizing agent comprises sodium ascorbate and water.

49. (Amended) The [nasally administered] pharmaceutical composition of Claim 39, wherein said [system] solubilizing agent comprises sodium metabisulfite and water.

50. (Amended) A [nasally administered] pharmaceutical composition for treating male erectile dysfunction in a mammal comprising a therapeutically effective amount of a dopamine receptor agonist which has been dispersed in [a system] an aqueous formulation for intranasal delivery comprising a stabilizing agent to improve [its] stability of said dopamine receptor agonist in the formulation.

51. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said dopamine receptor agonist is selected from the group consisting of apomorphine, chemically modified equivalents and pharmaceutical salts thereof.

52. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said [system] stabilizing agent comprises glycerin.

53. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said [system] stabilizing agent comprises a glycol derivative.

54. (Amended) The [nasally administered] pharmaceutical composition of Claim 53, wherein said glycol derivative is propylene glycol.

55. (Amended) The [nasally administered] pharmaceutical composition of Claim 53, wherein said glycol derivative is polyethylene glycol.

56. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said [system] stabilizing agent comprises a sugar alcohol.

57. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said [system] stabilizing agent comprises propylene glycol and glycerin.

58. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said [system] stabilizing agent comprises polyethylene glycol 400.

59. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said [system] stabilizing agent comprises ascorbic acid and water.

60. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said [system] stabilizing agent comprises sodium ascorbate and water.

61. (Amended) The [nasally administered] pharmaceutical composition of Claim 50, wherein said [system] stabilizing agent comprises sodium metabisulfite and water.